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Safety concerns grow over pharmacy-mixed drugs

By Julie Appleby
USA TODAY

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And, like Copeland, tens of thousands of those patients — and their doctors — may not know that they are using respiratory drugs that are mixed together in pharmacies from bulk-purchased ingredients: Those drugs are not approved by the Food and Drug Administration, and they are made with far less oversight than drugs produced by pharmaceutical companies.

At their best, such pharmacies produce a variety of medications for individual patients who can't get what they need from products made by brand-name or generic drug companies, such as flavored syrups for those who can't take pills and dye-free products for patients allergic to colorings.

Patients taking medicines for asthma, emphysema are said to be at risk

Cover story

Vial: Will Copeland's compounded drug.

But at worst, critics and regulators say, some pharmacies are skirting federal law by mass-producing drugs without FDA oversight, sometimes making contaminated, ineffective or too-potent products.

Because the state-regulated pharmacies are not held to the same quality and safety rules as FDA-regulated drug companies, they don't have to test their ingredients. And — in the overwhelming majority of states — they don't have to check the final products for potency or sterility. Nor are they required to report problems with their drugs.

"When you can know more about a box of Cheerios than you can about products some of these pharmacies are making, that's wrong," says Nancy Sander, president and founder of Allergy & Asthma Network Mothers of Asthmatics, an advocacy group based in Fairfax, Va.

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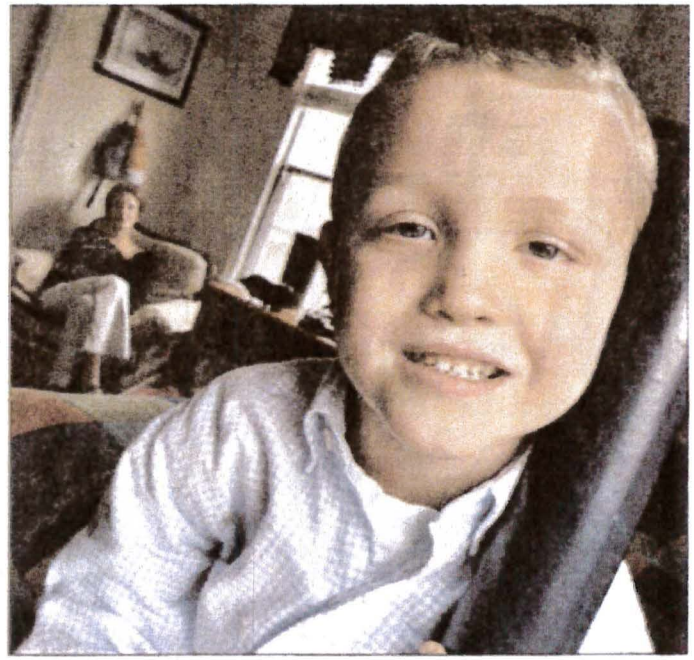

Photos by Sara D. Davis for USA TODAY

Asthma: Will Copeland's mother, Margaret, rear, says his medicine was switched to a pharmacy-mixed drug.

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Like millions of Americans, Margaret Copeland's 5-year-old son, Will, relies on prescription medications for his asthma and inhales the drugs daily with the help of a small, tabletop machine.

And, like Copeland, tens of thousands of those patients -- and their doctors -- may not know that they are using respiratory drugs that are mixed together in pharmacies from bulk-purchased ingredients: Those drugs are not approved by the Food and Drug Administration, and they are made with far less oversight than drugs produced by pharmaceutical companies.

At their best, such pharmacies produce a variety of medications for individual patients who can't get what they need from products made by brand-name or generic drug companies, such as flavored syrups for those who can't take pills and dye-free products for patients allergic to colorings.

But at worst, critics and regulators say, some pharmacies are skirting federal law by mass-producing drugs without FDA oversight, sometimes making contaminated, ineffective or too-potent products.

Discussion Questions

1. Should compounding pharmacies be under FDA oversight? Why or why not?
2. How might regulations be changed to allow compounding pharmacies to continue to make drugs while protecting patients and ensuring the efficacy of these products? Should any future regulations be left up to states to handle individually or should the federal government mandate new standards? Explain.
3. Discuss the recent changes in the way Medicare pays for respiratory drugs. Include likely affects on patients, taxpayers, traditional pharmacies and compounding pharmacies.

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The firms, called compounding pharmacies, make a wide variety of drugs , from dermatological treatments to injectable painkillers. While compounding technically violates federal drug law because pharmacies produce drugs without FDA approval, regulators have long allowed it because "the vast majority of pharmacies . . . provide a valuable medical service," Steven Galson, the FDA's acting director for the Center for Drug Evaluation and Research, told Congress in 2003.

But the agency has become increasingly concerned that some of these pharmacies are acting as drug manufacturers, producing millions of doses of medication, "which can expose large numbers of patients to health risks associated with unsafe or ineffective medications," Galson said.

No one knows exactly how many compounding pharmacies exist, but the FDA estimates that there are at least 3,000, and they make a minimum of 30 million prescriptions annually.

While generally not chain drugstores, they range from small independents to pharmacies owned by large, publicly traded home care companies. Some advertise on television and can turn out thousands of doses a day.

Respiratory drug profit margins

The pharmacies have found a particularly lucrative niche in respiratory drugs , garnering profit margins that can hit 75% or more, according to one recent industry analysis. Those profits are possible because Medicare and other insurers pay more for the drugs than it costs pharmacies to make them.

But their success also has attracted increased scrutiny. Today, a coalition of doctors and consumer advocates, including Sander's group, will petition the FDA to require pharmacy -made respiratory drugs to carry labels stating the products are not FDA-approved and have not been tested for safety and efficacy.

The FDA issued strong warnings to two pharmacies in December. Regulators in Missouri may yank the license of a pharmacy they say failed to recall all of more than 2 million doses of respiratory drugs possibly contaminated with bacteria. And drugmaker Chiron this month reached a settlement with three pharmacies selling their versions of its patented antibiotic tobramycin. The pharmacies agreed to put a disclaimer in their marketing materials warning that compounded drugs are not evaluated by the FDA for safety or efficacy.

While no deaths from pharmacy -made respiratory drugs have been documented, there are concerns about the potency and sterility of the drugs :

* A Med 4 Home pharmacy in Kansas City, Mo., notified more than 19,000 patients nationwide that it was recalling respiratory drugs in 2003 after state regulators found bacterial contamination. The state's Board of Pharmacy is seeking disciplinary action against the pharmacy , which could mean fines, license suspension or revocation.

* Recent FDA tests on batches of respiratory drugs from one Puerto Rican pharmacy found the amounts in the vials didn't match what the labels said they contained.

* Pharmacy -made respiratory drugs analyzed last year by drugmaker AstraZeneca, which sells a product that is often copied by pharmacies, found four of the five samples failed potency tests. Officials at AstraZeneca declined to comment on the internal analysis, but the company has launched a doctor-education campaign about the differences between pharmacy -made and brand-name drugs .

Concern about respiratory drugs made by pharmacies is also driven by the injuries and deaths associated with other types of compounded prescription drugs . The FDA knows of more than 200 adverse events caused by compounded drugs since 1990, including three deaths from an injectable painkiller and 13 hospitalizations, according to congressional testimony from 2003. And state regulators are investigating the January death of a North Carolina college student who was given a pharmacy -made skin anesthetic to use before a laser-hair-removal treatment.

Suspicions prove true

Patients say they often don't know they are getting pharmacy -made drugs .

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After switching pharmacies last year to one that offered a lower price on the asthma drug her son Will uses, Copeland says she became suspicious because the drug looked and smelled different. She called the pharmacy and was told the drug wasn't Pulmicort Respules, the brand-name drug made by AstraZeneca that her son had been taking. Instead, the pharmacist told her, it was a generic.

But there is no FDA-approved generic for Pulmicort. Generics differ from compounded drugs in that they must receive FDA approval and are made in plants under FDA oversight, while compounded drugs are not.

"I'm mad," says Copeland of Winston-Salem, N.C. "I received a product that was not what it was supposed to be. This drug is a lifesaving one for us. I can't have a wrong dose or a lower dose."

Pharmacies that make respiratory drugs say they fill a need by producing products in dosages not available commercially or by mixing several different types of drugs into single, more convenient vials. The drugs are taken with the help of a shoebox-size breathing machine called a nebulizer, which turns the liquid medication into a mist that can be inhaled. Patients often use it several times a day.

By combining several different drugs , patients can cut their nebulizer time from more than 20 minutes to seven, says Mickey Letson, owner of Letco Cos., which provides supplies and instruction on starting a compounding pharmacy . "That is a tremendous difference to a patient."

But some doctors say the 20 million Americans with asthma and chronic obstructive pulmonary disease (COPD) can be treated with a wide range of brand-name and generic drugs made by pharmaceutical companies; they have no need for compounded products. Industry critics say no one has tested whether combining several different drugs is safe or affects the potency of the products. Making the drugs , they add, is difficult to do under sterile conditions.

"Since we do have proven clinical products on the market, there is not a medical reason to create these compounded products, other than making a buck," says Philip Marcus, chief of pulmonary medicine at St. Francis Hospital in Roslyn, N.Y.

While some patients and their doctors choose drugs made by pharmacies so they can get special dosages or mixtures not commercially available, others don't know they are getting a compounded product.

Patients may send a prescription written for a brand-name drug to a pharmacy , perhaps attracted by advertisements for lower-cost drugs . The pharmacy then seeks permission from their doctors to switch them to compounded drugs .

"One day I get a delivery of my medicine, and I say, 'What's this?' It was different," says Shirley Scheyer, 74, of Boca Raton, Fla. Instead of two vials, she had one. Rather than having a brand-name manufacturer's label, it had a sticker on it listing the name of the drug.

Scheyer takes two medications -- albuterol and ipratropium -- to treat COPD, which becomes progressively worse over time. The new vials contained both drugs , which made it more convenient.

"It worked quicker, and that was definitely a plus," Scheyer says.

But Scheyer was still suspicious. "I started to worry about what I was putting into my impaired lungs," she says. "Is it free from bacteria? Their stuff may be perfectly all right, but it may not. I just don't know."

Tricky forms?

Some doctors say they are fooled into signing permission forms by pharmacies seeking to switch patients from brand-name products to their own medications.

Edward Kerwin, a board-certified respiratory specialist practicing in Oregon, says he always writes "do not compound, do not substitute" on his prescriptions. Pharmacies still try to get around that, he says, by faxing to his office misleading forms that authorize a switch to compounded products. One pharmacy faxed him four times in one month for the same patient prescription, he says.

"I think they hoped our busy office would just have me sign on the blank line," Kerwin said.

L.D. King, executive director of the International Academy of Compounding Pharmacists, a Houston-based non-profit association representing about 1,800 compounding pharmacies, says he has heard anecdotally about such efforts but has not seen forms that could be confusing. His group would not condone any such effort: "The physician should always know that it's a compounded medication."

Is compounding necessary?

All states and the FDA allow the compounding of drugs . But FDA officials are concerned that some pharmacies cannot match a manufacturer's ability to make and package complex drugs properly.

The FDA is also concerned about the difficulty in making sterile products in a pharmacy . Many respiratory drugs must be sterile because they are used by the very young, the very old and those with impaired lungs.

"Because of the requirements and nature of sterile products, they are the most difficult to prepare, and the consequences of error are most severe," says an FDA paper on compounding pharmacies published in 2000.

Proponents say compounding pharmacies overall are safe.

"There has not been one recorded death associated with nebulizer medications, to my knowledge, of the hundreds of millions of doses that have been compounded," says Letson of Letco Cos.

But a lawsuit filed in a Missouri court by the family of Robert Sparks alleges that the 70-year-old died in March 2003 after using medications made by the Med 4 Home pharmacy that were eventually recalled. The recalled drugs included albuterol/ipratropium combinations and budesonide.

Sparks, of Ceresco, Mich., used respiratory drugs to treat a chronic lung condition, says his lawyer, Richard Miller, of Kansas City, Mo. The lawsuit alleges that the drug was made negligently and not tested for sterility. Med 4 Home's Kansas City lawyers referred calls to parent company Lincare's general counsel at the company headquarters in Clearwater, Fla. The counsel did not return several calls.

Tracking problems associated with compounded medications is difficult because the overwhelming majority of states don't require compounding pharmacies to report adverse events associated with their products, according to the National Association of Boards of Pharmacy .

Several states are tightening their rules overseeing firms that compound drugs , even as it remains unclear where state authority ends and FDA oversight begins.

While regulating pharmacies is a state function, the FDA has stepped in when it decides a pharmacy has become a drug manufacturer.

But that line is unclear.

Compounding pharmacies argue that they are not under FDA jurisdiction as long as they have legitimate prescriptions from doctors, no matter whether they are making 20 doses or 20,000. Two cases challenging the FDA's authority are currently in court.

"State-licensed and compliant pharmacies may not be inspected by the FDA," says Howard Hoffmann, who filed a lawsuit against the FDA in September on behalf of compounding pharmacies in six states.

FDA oversight and rules could drive some pharmacies out of business with expensive and unnecessary requirements, industry supporters say. That would hurt patients who need specialized medication.

But patient advocates disagree, saying the pharmacies should be under FDA oversight, especially when they are large enough to make thousands of doses.

At the least, they say, patients and doctors need to be specifically informed that they are getting pharmacy -made drugs so they can weigh the drugs ' risks against their benefits. "Americans expect that if they're taking a prescribed medication that it's FDA approved," says Sander of the allergy mothers group. "That expectation is no longer ours to have."

Medicare cuts may not hurt compounding pharmacies

Medicare this year cut payments for respiratory drugs by almost 90%, driven by concerns that the program had long overpaid for the medications and growing criticism that some pharmacies are switching patients to pharmacy -made drugs to reap large profits.

Pharmacy -made prescription drugs are allowed when patients can't get what they need from commercially available products. But critics say large payments from Medicare and other insurers led some pharmacies to switch patients from brand-name drugs to their own versions.

That's because the payments to pharmacies are far larger than the costs involved for pharmacies to buy the ingredients and make the drugs . Also, unlike pharmaceutical companies, pharmacies don't have to absorb costs for research, development or testing of the drugs , because they generally do none of those things.

But, in January, Medicare changed the way it pays for respiratory drugs , cutting pharmacy payments by as much as 90%. Medicare officials say the change should reduce costs to taxpayers -- and may cut down on the number of pharmacies making their own versions of products.

Some pharmacy supporters say the cuts are drastic and could bankrupt some. Mickey Letson, whose company sells information

and supplies to compounding pharmacies, says the new rules mean pharmacies will likely only offer more expensive, brand-name drugs -- and patient co-payments could rise as a result.

"Medicare has backed everyone into a corner," says Letson.

But other pharmacy groups say pharmacy compounding of respiratory drugs remains profitable, despite the 90% cut.

An online newsletter from Respiratory Distributors -- a firm that sells compounding supplies -- estimated that gross profit margins under the new Medicare rules still range from 78% to 82% for some common respiratory drug combinations. "We still think that compounding will be a profitable part of any pharmacy operation," the newsletter said.